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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,325	01/29/2004	Theodora S. Ross	UM-08737	5496

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MEDLEN & CARROLL, LLP
Suite 350
101 Howard Street
San Francisco, CA 94105

EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/767,325	**Applicant(s)** ROSS ET AL.	
	Examiner Brandon J. Fetterolf, PhD	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05 January 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *see office action*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1 and 4-11*.
   Claim(s) withdrawn from consideration: *12-15*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

SHANON FOLEY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

DETAILED ACTION

Response to the Amendment

The Amendment filed on 1/05/2007 in response to the previous Final Office Action (10/31/2006) is acknowledged, but has not been entered. The amendment has not been entered because the amended claims recite limitations that have not been previously considered and as such, they raise new issue that would require further consideration under 112, 2nd paragraph, as well as 112, 1st paragraph new matter.

Claims 1 and 4-15 are currently pending.

Claims 12-15 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1 and 4-11 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

As Applicant's arguments appear to be solely drawn to the amendment which has not been entered, such arguments have not been considered. Therefore, all rejections are maintained as set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-11 remain rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between he steps. See MPEP § 2172.01. The omitted steps are: a correlation step describing how the results of the method relate back to the preamble of the method objectives.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are broadly drawn to a method for detecting cancer, comprising providing a sample from a subject suspected of having cancer and detecting the presence or absence of antibodies to HIP1, wherein the presence of antibodies to HIP1 is indicative of cancer. Thus, the claims imply that the presence or absence of antibodies to HIP1 in any sample can be used to detect any and/or all cancers.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to detecting any and/or all cancers comprising providing a sample from a subject suspected of having cancer; and detecting the presence or absence of antibodies to HIP1 in said sample, wherein the presence of antibodies to HIP1 is indicative of cancer. The specification teaches (page 36, lines 1-

10) that experiments conducted during the course of development of the present invention have demonstrated that subjects with prostate cancer preferentially exhibit a humoral response to HIP1. For example, the specification provides (page 83, lines 10-14) a humoral response to HIP1 in a TRAMP mouse model for prostate cancer, wherein 10/20 Tag positive TRAMP mice had antibodies in their serum to HIP1 whereas 0/10 normal Tag negative mice had antibodies in their serum to HIP1. In addition to the TRAMP mouse model, the specification teaches (page 82, Example 8) a humoral response to HIP1 in human prostate cancer patients, wherein 5/20 were positive for a humoral response to HIP1 in the prostate cancer patient cohort whereas 9/23 were positive in the "normal" patient cohort. Thus, while the specification appears to imply a nexus between a correlation between cancer detection and autoantibody presence to HIP1 in the TRAMP mouse model, the specification does not appear to clearly indicate whether or not antibodies to HIP1 is indicative of the cancerous state in a cancer patient. In other words, what may be "preferable" in the lab is only suggestive and does not qualify as a reasonable expectation of success, especially in a highly unpredictable art such as detecting the presence or absence of cancer. In the instant case, the TRAMP mouse model is an art recognized transgenic model of prostate cancer, which recapitulates many of the features of prostate cancer in humans (*see* Gupta, S. International Journal of Oncology 2004; 25: 1133-1148). For example, Gupta discusses that the TRAMP model has been used for a wide range of studies including the analysis of growth factors, assessment of intermediate and endpoint markers, markers of angiogenesis, and for evaluating the efficacy of natural agents and synthetic compounds in chemoprevention and therapy of prostate cancer (page 1138, 2nd column, beginning on the bottom to page 1140, 1st column). Thus, while the prior art teaches that the TRAMP mouse model is useful for a variety of studies, the art is silent with regards to the production of a humoral response to a specific cancer related antigen and using these results as a diagnostic marker for cancer. Furthermore, if a molecule such as an antibody to HIP1 is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some type of pattern that would allow the claimed antibody to be used in a diagnostic manner. For example, antibodies to HIP1 were found in serum of "normal" patients, as well as patients suffering from prostate cancer as evidenced by the disclosure (page 82, Example 2). Similarly, the specification teaches (page 63, lines 1+) that many proteins such as HIP1 are expressed in normal tissues and diseased tissues. Therefore, one needs to know that antibodies to HIP1 are

present only in a cancer patient to the exclusion of normal patients. Thus, in the absence of any correlation between antibodies to HIP1 with any known disease or disorder, any information obtained from various profiles in both normal and diseased tissue only serves as the basis for further research on the observation itself. Therefore, absent evidence of the antibodies to HIP1 presence including the correlation to a diseased state, one of skill in the art would not be able to predictably use antibodies to HIP1 in any diagnostic setting without undue experimentation.

Reasonable correlation must exist between the scope of the claims and the scope of the enablement set forth. In view of the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Therefore, NO claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHANON FOLEY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642